

6.

Mutagenic Evaluation of Compound FDA 73-87 (Sodium Alginate)

6/15/75

[REDACTED] /R

{ {

LBI PROJECT #2468

MUTAGENIC EVALUATION OF

COMPOUND FDA 73-87

PM9005383

SODIUM ALGINATE

SUBMITTED TO

FOOD & DRUG ADMINISTRATION
DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
ROCKVILLE, MARYLAND

SUBMITTED BY

LITTON BIONETICS, INC.
5516 NICHOLSON LANE
KENSINGTON, MARYLAND

JUNE 15, 1975



BIONETICS

TABLE OF CONTENTS

	Page No.
EVALUATION SUMMARY.....	1
I. <u>OBJECTIVE</u>	2
II. <u>MATERIALS</u>	2
A. Test Compound.....	2
B. Indicator Microorganisms.....	2
C. Reaction Mixture.....	2
D. Tissue Homogenates and Supernatants.....	3
E. Positive Control Compounds.....	3
III. <u>METHODS</u>	3
A. Toxicity.....	3
B. Plate Tests.....	4
C. Suspension Tests.....	4
D. Preparation of Tissue Homogenates and 9,000 x g Cell Fractions.....	5
E. Data Recording and Reporting.....	5
IV. <u>RESULTS SECTION</u>	6
A. Solubility Properties of the Test Compound.....	6
B. Toxicity and Dosage Determinations for the Test Compound.....	6
V. <u>SUMMARY OF TEST RESULTS</u>	7
VI. <u>INTERPRETATION OF RESULTS AND CONCLUSIONS</u>	14
A. <u>Salmonella typhimurium</u>	14
B. <u>Saccharomyces cerevisiae</u>	14
C. Conclusions.....	14
APPENDIX-TABULATION OF DATA.....	A-1



BIONETICS

EVALUATION SUMMARY

Compound FDA 73-87, Sodium Alginate, did not exhibit genetic activity in any of the in vitro microbial assays employed in this evaluation.



BIONETICS

Litton

DATE: June 15, 1975

SPONSOR: Food and Drug Administration, Contract Number 223-74-2104

SUBJECT: Evaluation of Test Compound PM9005383, Sodium Alginate FDA 73-87

I. OBJECTIVE

The objective of this study was to evaluate the test compound for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations.

II. MATERIALS

A. Test Compound

1. Date Received: August, 1974
2. Description: Fine white powder

B. Indicator Microorganisms

The following strains of indicator microorganisms were used in the evaluation:

Yeast Strain: Saccharomyces cerevisiae, strain D4

Bacteria Strains: Salmonella typhimurium, strains: TA-1535
TA-1537
TA-1538

C. Reaction Mixture

The following reaction mixture was employed in the activation tests:

<u>Component</u>	<u>Final Concentration/ml</u>
1. TPN (sodium salt)	6 μM
2. Isocitric acid	49 μM
3. Tris buffer, pH 7.4	28 μM
4. MgCl_2	1.7 μM
5. Tissue homogenate fraction	72 mg



BIONETICS

D. Tissue Homogenates and Supernatants

The tissue homogenates and 9,000 x g supernatants were prepared from tissues of the following mammalian species: Mouse-ICR random bred adult males; rat-Sprague-Dawley adult males; and primate-Macaca mulatta adult males.

E. Positive Control Compounds

Table 1 lists chemicals for positive controls in the direct and activation assays.

TABLE 1

POSITIVE CONTROLS USED IN DIRECT AND ACTIVATION ASSAYS

<u>Assay</u>	<u>Chemical^a</u>	<u>Solvent</u>	<u>Probable Mutagenic Specificity</u>
Nonactivation	Ethyl methanesulfonate	Water or saline	BPS ^b
	2-Nitrofluorene	Dimethylsulfoxide ^c	FS ^b
	Quinacrine mustard	Water or saline	FS
Activation	Dimethylnitrosamine	Water or saline	BPS ^b
	2-Acetylaminofluorene	Dimethylsulfoxide ^c	FS ^b

^a Concentrations given in the Results Section

^b BPS = base-pair substitution; FS = frameshift

^c Previously shown to be non-mutagenic

III. METHODS

A. Toxicity

The solubility, toxicity and doses for all chemicals were determined prior to screening.

Each chemical was tested for survival against the specific indicator strains over a range of doses to determine the 50% survival dose. Bacteria were tested in phosphate buffer, pH 7.4, for one hour at 37°C on a shaker. Yeasts were tested in phosphate buffer, pH 7.4, for four hours at 30°C on a shaker. The 50% survival curve and the 1/4 and 1/2 50% doses calculated.

If no toxicity was obtained for a chemical with a given strain, then a maximum dose of 5% (w/v) was used against the strain.

Unless otherwise specified, the doses calculated for the tests in buffer were applied to the activation tests. The solubility of the test chemical under treatment conditions is stated in the Results Section.



BIONETICS

B. Plate Tests

In the nonactivation procedure, approximately 10^9 cells of a log phase culture of the bacterial indicator strains were spread over the surface of a minimal plate, and a measured amount of the test chemical was placed in the center of the test plate. In activation tests, the test chemical was added to the cells, and an aliquot of the mixture was spread on the surface of the test plate. The reaction mixture (0.1 ml) plus tissue extract was then spotted on the surface of the plate. Positive and solvent controls were included. All plates were incubated at 37°C for four days and then scored. Each compound (Test, Positive Control and Solvent Control) was done in duplicate. Concentrations of the positive control compounds are listed in the Results Section.

C. Suspension Tests

1. Nonactivation

Log-phase bacteria and stationary-phase yeast cultures of the indicator organisms were grown in complete broth, washed and resuspended in 0.9% saline to densities of 1×10^9 cells/ml and 5×10^7 cells/ml, respectively. This constituted the working stock for tests of a group of test chemicals and their respective controls. Tests were conducted in plastic tissue culture plates. Cells plus appropriate volume(s) of the test chemical were added to the wells to give a final volume of 1.5 ml. The solvent replaced the test chemical in the negative controls. Treatment was at 30°C for four hours for yeast tests and at 37°C for one hour for bacterial tests. All flasks were shaken during treatment. Following treatment, the plates were set on ice. Aliquots of cells were removed, diluted in sterile saline (4°C) and plated on the appropriate complete media. Undiluted samples from flasks containing the bacteria were plated on minimal selective medium in reversion experiments. Samples from a 10^{-1} dilution of treated cells were plated on the selected media for enumeration of gene conversion with strain D4. Bacterial plates were scored after incubation for 48 hours at 37°C. The yeast plates were incubated at 30°C for 3-5 days before scoring.

2. Activation

Bacteria and yeast cells were grown and prepared as described in the nonactivation tests. Measured amounts of the test and control chemicals plus 0.25 ml of the stock-cell suspension were added to wells of the Linbro plate containing the appropriate tissue fraction and reaction mixture. All flasks (bacteria and yeast) were incubated at 37°C in an oxygen atmosphere with shaking. The treatment times as well as the dilutions, plating procedures and scoring of the plates were the same as described for nonactivation tests.



BIONETICS

D. Preparation of Tissue Homogenates and 9,000 x g Cell Fractions

Male animals (sufficient to provide the necessary quantities of tissues) were killed by cranial blow, decapitated and bled. Organs were immediately dissected from the animal using aseptic techniques and placed in ice-cold 0.25 M sucrose buffered with Tris at pH of 7.4. Upon collection of the desired quantity of organs, they were washed twice with fresh buffered sucrose and completely homogenized with a motor-driven homogenizing unit at 4°C. The whole organ homogenate obtained from this step was divided into two samples. One sample was frozen at -80°C and the other was centrifuged for 20 minutes at 9,000 x g in a refrigerated centrifuge. The supernatant from the centrifuged sample was retained and frozen at -80°C. These two frozen samples were used for the activation studies.

E. Data Recording and Reporting

Following the specified incubation periods all population plates were scored by an automatic colony counter and the results from each plate of a set were recorded, in ink, on data processing forms. All minimal or other types of selective media plates were hand scored and the results recorded along with the respective population data. Other relevant experimental data were recorded on experimental definition forms. For bacteria strains the number of colonies recorded from either the population or selective plates represents that number in 1 ml of test suspension plated. The numbers recorded for the yeast strain D4 represent the number in 0.5 ml of test suspension plated. The data were then processed and printed from a computer program.



BIONETICS

IV. RESULTS SECTION

A. Solubility Properties of the Test Compound

1. Name or code designation of the test compound: PM9005383
Sodium Alginate
2. Test solvent: DMSO
3. Solubility of the test compound under treatment conditions:
Insoluble under treatment conditions
4. Additional comments: Fine white powder

B. Toxicity and Dosage Determinations for the Test Compound

1. Test date for toxicity determination: March 25, 1975
2. The 50% survival level was determined for bacteria and yeast indicator organisms by conducting survival curves with the test compound at the following concentrations:

Percent Concentration (w/v or v/v)

5.0
0.5
0.05
0.005
0.0005

3. Concentrations of the test compound used in the mutagenicity tests:

<u>Dose</u>	<u>Percent Concentration</u>	
	<u>Bacteria</u>	<u>Yeast</u>
1/4 50% Survival	1.25	1.25
1/2 50% Survival	2.50	2.50
50% Survival	5.00	5.00
Plate Tests	2.50	--



BIONETICS

V. SUMMARY OF TEST RESULTS

Plate Tests

A. Name or code designation of the test compound: PM9005383

B. Test date: April 30, 1975

C. Concentration of the test compound: 2.5%

Test	Species	Tissue	Revertants/Plate					
			TA-1535		TA-1537		TA-1538	
			1	2	1	2	1	2
1. Nonactivation								
Solvent Control	---	---	138	146	25	22	26	35
Positive Control ^a	---	---	>10 ⁴	>10 ⁴	193	176	158	219
Test Compound	---	---	134	151	19	18	32	44
2. Activation								
Negative Control	---	---	56	74	9	25	28	16
Solvent Control	---	---	44	84	46	41	44	39
Reaction Mixture Control	---	---	83	72	35	42	30	43
Positive Control ^b	Mouse	Liver	>10 ³	>10 ³	86	94	332	341
Positive Control		Lung	96	87	9	11	43	80
Positive Control		Testes	84	121	10	17	22	26
Positive Control	Rat	Liver	10	10	85	86	382	310
Positive Control		Lung	87	72	8	14	27	21
Positive Control		Testes	84	116	11	15	19	36
Positive Control	Monkey	Liver	345	339	93	88	340	364
Positive Control		Lung	81	73	11	10	14	24
Positive Control		Testes	87	115	9	19	19	28
Test Compound	Mouse	Liver	29	15	42	40	14	18
Test Compound		Lung	21	14	14	11	24	27
Test Compound		Testes	23	32	10	8	22	2
Test Compound	Rat	Liver	24	15	31	32	22	13
Test Compound		Lung	22	22	12	7	20	18
Test Compound		Testes	29	43	15	11	16	8
Test Compound	Monkey	Liver	22	13	28	32	16	15
Test Compound		Lung	19	12	8	10	16	17
Test Compound		Testes	25	29	15	9	18	2
^a	TA-1535	EMS	10 μ l/plate		^b TA-1535	DMNA	50 μ M/plate	
	TA-1537	QM	20 μ g/plate			TA-1537	AAF	100 μ g/plate
	TA-1538	NF	100 μ g/plate			TA-1538	AAF	100 μ g/plate



BIONETICS

DATA TABLE TERMS AND ABBREVIATIONS

<u>ABBREVIATION OR TERM</u>	<u>DEFINITION OR EXPLANATION</u>																																
COMPOUND	Client designated compound number appears in this column.																																
TEST CODES	<table style="margin-left: 20px;"> <tr><td>NAN</td><td>= Nonactivation: Solvent Control</td></tr> <tr><td>NAP</td><td>= Nonactivation: Positive Control</td></tr> <tr><td>NA1</td><td>= Nonactivation: Test Compound Dose 1</td></tr> <tr><td>NA2, etc.</td><td>= Reflects the other dose level(s)</td></tr> <tr><td> </td><td></td></tr> <tr><td>A+C</td><td>= Negative Chemical Control</td></tr> <tr><td>A-C</td><td>= Activation: Solvent Control</td></tr> <tr><td>ACP</td><td>= Activation: Positive Control</td></tr> <tr><td>ACT</td><td>= Activation: Test Compound</td></tr> <tr><td>A+T</td><td>= Activation: Tissue Control</td></tr> <tr><td> </td><td></td></tr> <tr><td>LI</td><td>= Liver Tissue Activation Fraction</td></tr> <tr><td>LU</td><td>= Lung Tissue Activation Fraction</td></tr> <tr><td>KI</td><td>= Kidney Tissue Activation Fraction</td></tr> <tr><td>TE</td><td>= Testes Tissue Activation Fraction</td></tr> <tr><td>1,2, etc.</td><td>= Dose Levels</td></tr> </table>	NAN	= Nonactivation: Solvent Control	NAP	= Nonactivation: Positive Control	NA1	= Nonactivation: Test Compound Dose 1	NA2, etc.	= Reflects the other dose level(s)	 		A+C	= Negative Chemical Control	A-C	= Activation: Solvent Control	ACP	= Activation: Positive Control	ACT	= Activation: Test Compound	A+T	= Activation: Tissue Control	 		LI	= Liver Tissue Activation Fraction	LU	= Lung Tissue Activation Fraction	KI	= Kidney Tissue Activation Fraction	TE	= Testes Tissue Activation Fraction	1,2, etc.	= Dose Levels
NAN	= Nonactivation: Solvent Control																																
NAP	= Nonactivation: Positive Control																																
NA1	= Nonactivation: Test Compound Dose 1																																
NA2, etc.	= Reflects the other dose level(s)																																
A+C	= Negative Chemical Control																																
A-C	= Activation: Solvent Control																																
ACP	= Activation: Positive Control																																
ACT	= Activation: Test Compound																																
A+T	= Activation: Tissue Control																																
LI	= Liver Tissue Activation Fraction																																
LU	= Lung Tissue Activation Fraction																																
KI	= Kidney Tissue Activation Fraction																																
TE	= Testes Tissue Activation Fraction																																
1,2, etc.	= Dose Levels																																
CONCENTRATION	<p>All test compound dose levels are expressed as a whole number followed by an exponent (negative) identified by the appropriate units.</p> <p>Example: 0025-2PCT = 0.25 percent concentration</p>																																
POPU	Total number of viable cells in the plating sample raised to some exponent printed directly below the abbreviation (i.e., EP + 6 = $\times 10^6$).																																
MUT 1	Total number of mutants or convertants obtained from the sample plated raised to some exponent printed directly below the abbreviation (i.e., EP + 0 = 10^0). For strain D4, MUT 1 represents the number of ADE+ convertants.																																
MUT 2	Only used for strain D4 and represents the number of TRY+ convertants in the plated sample.																																
FREQ 1	The calculated mutation or gene conversion frequency times the negative exponent written directly below. For strain D4, FREQ 1 represents the ADE+ value.																																
FREQ 2	Only used for strain D4 and represents the TRY+ conversion frequency.																																
CONTAM	Presence of contamination on any plates.																																



BIONETICS

DATA TABLE TERMS AND ABBREVIATIONS (continued)

<u>ABBREVIATION OR TERM</u>	<u>DEFINITION OR EXPLANATION</u>
AAF	2-Acetylaminofluorene
DMSO	Dimethylsulfoxide
DMN	Dimethylnitrosamine
EMS	Ethyl Methanesulfonate
QM	Quinacrine Mustard
NF	Nitrofluorene
SPECIES	Animal Strains
SPRDAW	Sprague Dawley Rats
ICRFLO	Flow ICR Random Bred Mice
RHESUS	Rhesus Monkey (<u>Macaca mulatta</u>)
MIXEDB	Dog, Mixed Breed
NEWZEA	New Zealand White Rabbit



BIONETICS

LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 07/08/75

SPECIES

COMPOUND PM9005383

TEST	ORG	TA1537 HIS EX-8	TA1538 HIS EX-8	TA1535 HIS EX-8	0000D4 ADE EX-5	0000D4 TRY EX-5
NAN		5.32	1.24	12.94	1.89	1.48
NAP		1764.20	922.93	771.32	129.05	155.87
NA1		6.27	0.37	5.54	0.36	0.18
NA2		5.05	1.81	8.65	2.02	0.22



BIONETICS

LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 07/08/75

SPECIES ICRFLO/MOUSE

COMPOUND PM9005383

TEST	ORG	TA1537 HIS EX-8	TA1538 HIS EX-8	TA1535 HIS EX-8	0000D4 ADE EX-5	0000D4 TRY EX-5
ACT	A+C	20.45	6.88	3.23	2.25	1.59
ACT	A+T	35.90	6.31	7.69	3.25	1.59
ACT	A-C	12.22	2.93	3.73	0.96	0.17
ACT	PLI	45.07	15.26	5496.88	7.59	6.16
ACT	PLII	20.50	4.48	4.79	2.42	2.60
ACT	PTE	28.79	2.33	9.15	3.81	2.06
ACT	LI1	4.16	0.52	0.27	1.35	4.95
ACT	LI2	10.33	3.75	0.59	2.73	1.42
ACT	LU1	11.56	1.67	0.93	1.35	2.51
ACT	LU2	11.53	0.24	0.93	1.52	2.03
ACT	TE1	1.86	0.43	1.52	1.35	0.68
ACT	TF2	9.22	2.81	2.72	1.32	1.61



BIONETICS

LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 07/08/75

SPECIES SPRDAW/RAT

COMPOUND PM9005383

TEST	ORG	TA1535 HIS EX-8	TA1537 HIS EX-8	TA1538 HIS EX-8	TA1535 HIS EX-8	000004 ADE EX-5	000004 TRY EX-5
ACT	A+C		10.86	4.75	4.48	2.85	1.11
ACT	A+T		10.31	6.57	2.48	2.43	1.66
ACT	A-C	25.59	8.87	9.05	5.52	2.68	1.44
ACT	PLI		17.19	20.33	333.15	4.50	4.42
ACT	PLU		14.09	8.76	6.11	2.49	1.03
ACT	PTE		11.40	6.77	8.60	3.24	1.66
ACT	L11	8.08	9.75	1.29		1.44	0.72
ACT	L12		10.57	1.26	2.22	2.06	2.29
ACT	L01	9.71	6.58	1.34		1.66	1.99
ACT	L02		17.29	4.83	8.09	1.02	1.42
ACT	TF1		11.31	1.67	6.05	1.77	0.89
ACT	TF2		11.28	3.02	5.55	1.17	1.57



BIONETICS

LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 07/08/75

SPECIES RHECUS/MONKEY COMPOUND PM9005383

TEST	ORG	TA1537 HIS EX-8	TA1535 HIS EX-8	TA1538 HIS EX-8	0000D4 ADE FX-5	0000D4 TRY EX-5
ACT	A+C	6.36	4.50	10.43	1.82	1.82
ACT	A+T	3.92	5.62	5.80	2.59	2.73
ACT	A-C	5.63	7.72	2.70	2.16	1.80
ACT	PLI	10.56	1194.98	54.55	6.38	3.75
ACT	PLU	5.60	5.81	5.22	2.40	2.64
ACT	PTE	8.26	3.99	6.61	5.41	2.30
ACT	L11	0.77	2.01	0.79	2.11	0.88
ACT	L12	1.69	2.78	2.65	1.53	1.15
ACT	LU1	0.16	0.98	1.15	1.90	0.95
ACT	LU2	1.16	2.29	2.38	1.64	1.20
ACT	TE1	1.01	3.55	1.21	0.78	1.24
ACT	TE2	1.56	2.98	2.78	2.04	1.63

VI. INTERPRETATION OF RESULTS AND CONCLUSIONS

Compound PM9005383, Sodium Alginate, was tested for genetic activity in a series of in vitro microbial assays with and without metabolic activation. The following results were obtained:

A. Salmonella typhimurium

1. Plate tests

At a concentration of 2.5%, PM9005383, was not mutagenic for any of the bacterial indicator strains with or without activation. A high number of spontaneous revertants were observed in the nonactivation test using TA-1535. This culture was replaced.

2. Nonactivation suspension tests

The results of these tests were negative.

3. Activation suspension tests

The results of these tests were negative. Due To the insolubility of the compound, no results were obtained from initial tests at L11 and L11 dose levels with TA-1535 using rat tissue. Repeat tests were negative.

B. Saccharomyces cerevisiae

1. Nonactivation suspension tests

The results of these tests were negative.

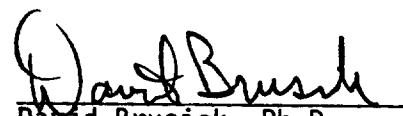
2. Activation suspension tests

The results of these tests were negative.

C. Conclusions

Test compound, Sodium Alginate, did not exhibit genetic activity in any of the assays employed in this investigation.

Submitted by:



David Brusick, Ph.D.
Director of Genetics



BIONETICS

REPORT EXR33 LITTON BIONETICS MILITARY ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104

EXPERIMENT 509802 DEFECTOR TA1535 SPECIES /

PROJECT 02468 DATE - 07/08/75

COMPOUND	ORG	TEST ID	CONCENTRATION	P0P01	M0T1	F0F01	COUNTAM
NAN	SALINE		0487	0063	12.94	0	
NAP	EMSS	0.002 %	0537	4142	771.32	0	
PM9005383	NA1	0025-1 PCT.	0343	0019	5.54	0	
PM9005383	NA2	0125-2 PCT.	0370	0032	8.65	0	



BIONETICS

REPORT FXR33 LITTON BIONETICS MULTIGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT	CONTRACT	TEST	ORG	TEST ID	CONCENTRATION	SPECIES	PROJECT	DATE
511301	22374-2104	DETECTOR	TA1537	/	/	/	02468	07/08/75
COMPONENT		TEST	ID				FRF01	
NAN							FP+Q	
NAP				SALINE	0601	0032	FP-R	COUNTAM
PM9005383	NA1			OM 1.0 UG/ML	0257	4534	5.32	0
PM9005383	NA2			0025-1 PCT.	0542	0034	1764.20	0
				0125-2 PCT.	0653	0033	6.27	0
							5.05	0



BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT	CONTRACT	TEST	ORG	SPFCIFS	PROJECT	DATE
509803	22374-2104	DETECTOR	TA1538	/	02468	07/08/75
		IN	CONCENTRATION	P0P01 EP+6	MULTI FP+8	
NAN		DMSO		0563	0007	1.24
NAP	NF 125 UG-ML			0567	5233	0
PM9005383	NA1	0025-1 PCT.	0811	0003	922.93	0
PM9005383	NA2	0125-2 PCT.	0830	0015	0.37	0
					1.81	0



BIONETICS

REPORT EXR33 LITTON BIONETICS MAGNETIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 514705 CONTRACT 22374-2104

COMPOUND	TEST ID	CONCENTRATION	SPECIES			PROJECT 07468 /	DATE - 07/08/75	
			ORG	P0PHI	MULT1			MULT2
NAN	SALINE	FMS 1.0 %	0741	0014	0011	1.89	1.48	0
NAP		0179	0231	0279	129.05	155.87	0	
PM9005383	NA1	0025-1 PCT.	0556	0002	0001	0.36	0.18	0
PM9005383	NA2	0125-2 PCT.	0446	0009	0001	2.02	0.22	0



BIONETICS



BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

COMPOUND	TEST	IN	CONCENTRATION	P0P01	MUT1	FRF01	CONTAM
A+C	DNN	50 UM/ML	0650	0021	3.23	0	0
A+T	***NN MATCH***	0156	0012	7.69	0	0	0
A-C	SAL INF	0670	0025	3.73	1	1	1
ACP	LI	DNN 50 UM/ML	0096	5277	5496.88	0	0
ACP	LU	DNN 50 UM/ML	0313	0015	4.79	0	0
ACP	TE	DNN 50 UM/ML	0153	0014	0.15	0	0
PM9005383	ACT	LI1	0025-1 PCT.	0748	0002	0.27	0
PM9005383	ACT	LI2	0125-2 PCT.	0512	0003	0.59	0
PM9005383	ACT	LU1	0025-1 PCT.	0752	0007	0.93	0
PM9005383	ACT	LU2	0125-2 PCT.	0963	0009	0.93	0
PM9005383	ACT	TF1	0025-1 PCT.	0920	0014	1.52	0
PM9005383	ACT	TF2	0125-2 PCT.	1066	0029	2.72	2

REPORT FXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 517602 CONTRACT 22374-2104

DETECTOR TA1537 SPECIES ICRLn/MuLSE PROJECT 02468 DATE - 07/08/75

COMPOUND	ORG	ID	CONCENTRATION	PPPII	MUTL.	PPFO1	PP-R	CONTAM
A+C	AAF	800 UG/ML	0308	0063	20.45	0		
A+T	***NO MATCH**	0078	0028		35.90	1		
A-C	DMSO		0483	0059	12.22	0		
ACP	LI	AAF 800 UG/ML	0071	0032	45.07	1		
ACP	LU	AAF 800 UG/ML	0161	0033	20.50	0		
ACP	TE	AAF 800 UG/ML	0198	0057	28.79	0		
PM9005383	ACT	L11 0025-1 PCT.	0361	0015	4.16	0		
PM9005383	ACT	L12 0125-2 PCT.	0184	0019	10.33	0		
PM9005383	ACT	L11 0025-1 PCT.	0294	0034	11.56	0		
PM9005383	ACT	L12 0125-2 PCT.	0555	0064	11.53	0		
PM9005383	ACT	TF1 0025-1 PCT.	0698	0013	1.86	0		
PM9005383	ACT	TF2 0125-2 PCT.	0347	0037	9.22	0		



BIONETICS



BIONETICS

REPORT FXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY HACCIUP DETAIL

CONTRACT 22374-2104

EXPERIMENT 509701 DETECTOR TA153R

COMPOUND	TEST	NRG	ID	CONCENTRATION	SPECIES	ICRF _L /MINIF	PROJECT 07468	DATE - 07/08/75
A+C		AAF	800	UG/ML	0858	0059	6.88	0
A+T		***ND	MATCH***	0666	0042	6.31	0	0
A-C		DMSO		0819	0024	2.93	0	0
ACP	LI	AAF	800	UG/ML	0675	0103	15.26	0
ACP	LU	AAF	800	UG/ML	1026	0046	4.48	2
ACP	TE	AAF	800	UG/ML	0945	0022	2.33	0
PM9005383	ACT	LI1	0025-1	PCT.	0575	0003	0.52	2
PM9005383	ACT	LI2	0125-2	PCT.	0567	0021	3.75	0
PM9005383	ACT	LI1	0025-1	PCT.	1020	0017	1.67	2
PM9005383	ACT	LI2	0125-2	PCT.	0828	0002	0.24	2
PM9005383	ACT	TE1	0025-1	PCT.	1169	0005	0.43	2
PM9005383	ACT	TF2	0125-2	PCT.	0604	0017	2.81	2

REPORT FXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104			PROJECT 02468			DATE - 07/08/75		
EXPERIMENT 512601	DETECTOR 000004	SPECIES ICREFL0/MNUISF	ORG	PROBII	MUT1	MUT2	FREQ01	FREQ02
COMPUND TEST ID	CONECENTRATION		EP+4	EP+1	FP+1	FP+5	FP-5	CONTAM
A+C DMN 90 UM/ML	0755	0017	0017	2.25	1.59	0		
A+T ***ND WATCH***	1260	0041	0020	3.25	1.59	6		
A-C SALINE	1145	0011	0002	0.96	0.17	0		
ACP LI DMN 90 UM/ML	0909	0069	0056	7.59	6.16	6		
ACP LU DMN 90 UM/ML	1117	0027	0029	2.42	2.60	0		
ACP TE DMN 90 UM/ML	0970	0037	0020	3.81	2.06	6		
PM9005383 ACT L11 0025-1 PCT.	0222	0003	0011	1.35	4.95	3		
PM9005383 ACT L12 0125-2 PCT.	0844	0023	0012	2.73	1.42	4		
PM9005383 ACT L01 0025-1 PCT.	0517	0007	0013	1.35	2.51	2		
PM9005383 ACT L02 0125-2 PCT.	0984	0015	0020	1.52	2.03	0		
PM9005383 ACT TF1 0025-1 PCT.	0148	0002	0001	1.35	0.68	0		
PM9005383 ACT TF2 0125-2 PCT.	0684	0009	0011	1.32	1.61	4		



BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 510801			CONTRACT 22374-2104			PROJECT 02468			DATE - 07/08/75		
EXPERIMENT 510801			CONTRACT 22374-2104			SPECIFS SPRDAM/RAT			PROJECT 02468		
COMPUND	ORG	IND	CONCENTRATION	PPM	MJT	PPM	MJT	PPM	MJT	PPM	CONTAM
A+C	DNN	50 UM/ML	0692	0031				4.48			0
A+T	***NO MATCH***		0483	0012				2.48			3
A-C	SAL INF		0725	0040				5.57			0
ACP	L1	DNN 50 UM/ML	0368	1226				333.15			1
ACP	L0	DNN 50 UM/ML	0311	0019				6.11			0
ACP	TE	DNN 50 UM/ML	0349	0030				8.60			0
PM9005383	ACT	L12 0125-2 PCT.	0450	0010				2.22			2
PM9005383	ACT	L12 0125-2 PCT.	0556	0045				8.09			0
PM9005383	ACT	TF1 0025-1 PCT.	0248	0015				6.05			0
PM9005383	ACT	TF2 0125-2 PCT.	0613	0034				5.55			0



BIONETICS



BIONETICS

REPORT FXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 515703 CONTRACT 22374-2104
DETECTOR TA1535 SPECIES SPRDAM/RAT

COMPOUND	ORG	TEST ID	CONCENTRATION	POPUL.	MUTL.	PERCENT
	A-C		SALINE	2454	0628	26.59
PM9005383	ACT	LII	0025-1 PCT.	2995	0247	8.08
PM9005383	ACT	LII	0025-1 PCT.	2421	0235	9.71

PROJECT 02468

DATE - 07/08/75

2



BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 511501 CONTRACT 22374-2104 DETECTOR TA1537 PROJECT 02468

SPCIES SPRDAM/RAT DATE - 07/08/75

COMPUND	TFST	ORG	CONCENTRATION	POPUL	MUTL	FRFQ1	FRFQ2	CONTAM
A+C		AAF 800 ug/ml	0663	0072	10.86	0	0	0
A+T		***NO MATCH***	0446	0046	10.31	0	0	0
A-C		DMSO	0688	0061	8.87	0	0	0
ACP	LI	AAF 800 ug/ml	0512	0088	17.19	2	0	0
ACP	LU	AAF 800 ug/ml	0589	0083	14.09	0	0	0
ACP	TE	AAF 800 ug/ml	0544	0062	11.40	0	0	0
PM9005383	ACT	LI1 0025-1 PCT.	0523	0051	9.75	2	0	0
PM9005383	ACT	LI2 0125-2 PCT.	0331	0035	10.57	2	0	0
PM9005383	ACT	LI1 0025-1 PCT.	0593	0039	6.58	0	0	0
PM9005383	ACT	LI2 0125-2 PCT.	0376	0065	17.29	0	0	0
PM9005383	ACT	TF1 0025-1 PCT.	0442	0050	11.31	0	0	0
PM9005383	ACT	TF2 0125-2 PCT.	0390	0044	11.28	0	0	0

REPORT FXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPUND SUMMARY BACKUP DETAIL

EXPERIMENT 511801 CONTRACT 22374-2104
DETECTOR TA1538 PROJECT 07468
SPECIFS SPRDAM/RAT

COMPUND	TEST	ORG	IN	CONCENTRATION	PROT	MUT	FRF01	EP-R	CONTAM
A+C		AAF	800 UG/ML	0926	0044	4.075	0	0	
A+T		***NN MATCH***		0792	0052	6.57	0	0	
A-C		DMSO		0707	0064	9.05	0	0	
ACP	LI	AAF	800 UG/ML	0718	0146	20.33	2	0	
ACP	LU	AAF	800 UG/ML	0833	0073	8.76	0	0	
ACP	TE	AAF	800 UG/ML	0886	0060	6.77	?	0	
PM9005383	ACT	LII	0025-1 PCT.	0619	0008	1.29	0	0	
PM9005383	ACT	LII	0125-2 PCT.	0475	0006	1.26	0	0	
PM9005383	ACT	LII	0025-1 PCT.	0747	0010	1.34	0	0	
PM9005383	ACT	LII	0125-2 PCT.	0663	0032	4.083	0	0	
PM9005383	ACT	TF1	0025-1 PCT.	0720	0012	1.67	0	0	
PM9005383	ACT	TF2	0125-2 PCT.	0696	0021	3.02	0	0	



BIONETICS

REPORT EXR33 LITTON BIONETICS MAGNETIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 512501			CONTRACT 22374-2104			PROJECT 02468			DATE - 07/08/75		
DETECTOR 000004			SPECIES SPRDAM/RAT								
COMPOUND	TEST ID	ORG CONCENTRATION	P0P11 EP+4	M0T1 FP+T	M0T2 FP+1	FRE01 FP-5	FRE02 FP-5	COUNTAM			
A+C	DMN 90 UM/ML	1438	0041	0016	2.85	1.11	0				
A+T	***ND MATCH**	0906	0022	0015	2.43	1.66	7				
A-C	SALINE	1044	0028	0015	2.68	1.44	0				
ACP	LI DMN 90 UM/ML	1177	0053	0052	4.50	4.42	6				
ACP	LU DMN 90 UM/ML	1167	0029	0012	2.49	1.03	0				
ACP	TE DMN 90 UM/ML	1203	0039	0020	3.24	1.66	0				
PM9005383	ACT LI1 0025-1 PCT.	0139	0002	0001	1.44	0.72	2				
PM9005383	ACT LI2 0125-2 PCT.	0874	0018	0020	2.06	2.29	0				
PM9005383	ACT LU1 0025-1 PCT.	0301	0005	0006	1.66	1.99	0				
PM9005383	ACT LU2 0125-2 PCT.	0984	0010	0014	1.02	1.42	0				
PM9005383	ACT TF1 0025-1 PCT.	0903	0016	0008	1.77	0.89	2				
PM9005383	ACT TF2 0125-2 PCT.	0766	0009	0012	1.17	1.57	0				



BIONETICS

REPORT FXR33 LITTON BIONETICS MILITAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT	CONTRACT	TEST	ORG	ID	CONCENTRATION	SPECIES	RHF/SUS/MUNKFY	PROJECT NO/468	DATE - 07/08/75
509901	22374-2104	DETECTOR TA1535			PNP11	MIL1	FRF01		
			A+C	DMM 50 UM/ML	FP+6	FP+0	FP-R	CNTAM	
			A+T	***END MATCH***	0534	0030	4.50	0	
			A-C	SALINE	0479	0037	5.62	0	
			ACP	L1 DMM 50 UM/ML	0458	5473	7.72	1	
			ACP	L0 DMM 50 UM/ML	0551	0032	5.81	0	
			ACP	TE DMM 50 UM/ML	0426	0017	3.99	2	
			PM9005383	ACT L11 0025-1 PCT.	1792	0036	2.01	0	
			PM9005383	ACT L12 0125-2 PCT.	0826	0023	2.78	0	
			PM9005383	ACT L11 0025-1 PCT.	0711	0007	0.98	0	
			PM9005383	ACT L12 0125-2 PCT.	1046	0024	2.29	0	
			PM9005383	ACT TF1 0025-1 PCT.	1182	0042	3.55	0	
			PM9005383	ACT TF2 0125-2 PCT.	1176	0035	2.98	0	



BIONETICS



BIONETICS

REPORT FXR33 LITTON BIONETICS MAGNETIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL.

EXPERIMENT	CONTRACT	DETECTOR	TA1537	SPECIES	RHESUS/MONKEY	PROJECT 07468	DATE - 07/08/75
511901	22374-2104			PNP11	MUT1	FRF01	
		ID	CONCENTRATION	FP+6	FP+0	FP-8	CONTAM
A+C	AAF 800 UG/ML		0692	0044		6.36	0
A+T	***NO MATCH***		0638	0025		3.97	0
A-C	DMSO		0533	0030		5.63	0
ACP	L1	AAF 800 UG/ML	0606	0064		10.56	0
ACP	L0	AAF 800 UG/ML	0643	0036		5.60	0
ACP	TE	AAF 800 UG/ML	0545	0045		8.26	0
PM9005383	ACT	L11	0025-1 PCT.	0653	0005	0.77	0
PM9005383	ACT	L12	0125-2 PCT.	0649	0011	1.69	0
PM9005383	ACT	L01	0025-1 PCT.	0610	0001	0.16	0
PM9005383	ACT	L02	0125-2 PCT.	1465	0017	1.16	0
PM9005383	ACT	TF1	0025-1 PCT.	0890	0009	1.01	0
PM9005383	ACT	TF2	0125-2 PCT.	1156	0018	1.56	0

REPORT EXR33 LITTON BIONETICS MAGNETIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

EXPERIMENT 510001			CONTRACT 22374-2104	DETECTOR TA1538	SPECIFS RHFSUS/MNKFY	PROJECT 07468	DATE - 07/08/75
COMPOUND	TEST	ORG	IN	CONCFNTRATION	P0P01 EP+6	F0F01 FP+8	CNTAM
A+C				AAF 800 UG/ML	0748	0078	0
A+T				***NO MATCH***	0742	0043	0
A-C		DMSO			0742	0020	2
ACP	L	AAF 800 UG/ML		0638	0348	54.55	0
ACP	LU	AAF 800 UG/ML		0901	0047	5.22	0
ACP	TE	AAF 800 UG/ML		0681	0045	6.61	0
PM9005383	ACT	L11	0025-1 PCT.		1012	0008	0.79
PM9005383	ACT	L12	0125-2 PCT.		0830	0022	2.65
PM9005383	ACT	LH1	0025-1 PCT.		0953	0011	1.15
PM9005383	ACT	LH2	0125-2 PCT.		1135	0027	2.38
PM9005383	ACT	TF1	0025-1 PCT.		1072	0013	1.21
PM9005383	ACT	TF2	0125-2 PCT.		1081	0030	2.78



BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DFTAIL

CONTRACT 22374-2104
EXPERIMENT 514202 DETECTOR 000004 SPF C1FS RHFSUS/MNKEY

PROJECT 07468 DATE - 07/08/75

COMPOUND	TEST	ORG	CONCENTRATION	P0P11	MUT1	MUT2	FREQ1	FREQ2	CONTAM
		ID		EP+4	EP+1	FP+1	EP-5	FP-5	
A+C		DNN 90 UM/ML	0658	0012	0012	1.82	1.82	1.82	1
A+T		***NO MATCH***	0695	0018	0019	2.59	2.73	2.73	1
A-C		SALINE	0555	0012	0010	2.16	1.81	1.81	7
ACP	I.I	DNN 90 UM/ML	0799	0051	0030	6.38	3.75	3.75	0
ACP	L.U	DNN 90 UM/ML	0832	0020	0022	2.40	2.64	2.64	1
ACP	TE	DNN 90 UM/ML	0739	0040	0017	5.41	2.30	2.30	4
PM9005383	ACT	L11 0025-1 PCT.	0568	0012	0005	2.11	0.88	0.88	2
PM9005383	ACT	L12 0125-2 PCT.	0784	0012	0009	1.53	1.15	1.15	4
PM9005383	ACT	L01 0025-1 PCT.	0737	0014	0007	1.90	0.95	0.95	0
PM9005383	ACT	L02 0125-2 PCT.	0916	0015	0011	1.64	1.20	1.20	1
PM9005383	ACT	TF1 0025-1 PCT.	0643	0005	0008	0.78	1.24	1.24	4
PM9005383	ACT	TF2 0125-2 PCT.	0736	0015	0012	2.04	1.63	1.63	1



BIONETICS